PATENT
674523-2021

AMENDMENT

Please amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows.

IN THE CLAIMS

1. (Currently Amended) A retroviral vector comprising:

(a) a 3' and 5' long terminal repeat (LTR);

(b) a functional splice donor site within the 5' LTR;

(c) a functional splice acceptor site;

(d) a first nucleotide sequence of interest (NOI) flanked upstream by the functional splice donor site and downstream by the functional splice acceptor site; and

(e) a second NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;

whereby the first NOI is spliced out of RNA transcribed from the retroviral vector ~~removed as a result of splicing~~.

2-4. (Cancelled)

5. (Previously presented) The retroviral vector according to claim 1 wherein the second NOI encodes a therapeutic expression product.

6. (Currently amended) The retroviral vector according to claim 1 wherein the first NOI, or ~~the~~ an expression product thereof, comprises a selectable marker or a viral element.

7-8. (Cancelled)

9. (Previously presented) The retroviral vector according to claim 1 wherein the functional splice donor site is from a virus.

10. (Previously presented) The retroviral vector according to claim 1 wherein the functional splice donor site is from an intron.

11. (Previously presented) The retroviral vector according to claim 10 wherein the intron is the small t-intron of SV40 virus.

12-13. (Cancelled)

14. (Previously presented) The retroviral vector according to claim 1 further comprising a multiple cloning site, wherein the functional splice acceptor site is located upstream of the multiple cloning site.

15. (Previously presented) The retroviral vector according to claim 1 wherein the functional splice acceptor site is from a nucleotide sequence coding for an immunological protein.

16. (Previously presented) The retroviral vector according to claim 15 wherein the immunological protein is an immunoglobulin.

17. (Previously presented) The retroviral vector according to claim 16 wherein the immunoglobulin is from an immunoglobulin heavy chain variable region.

18-20. (Cancelled)

21. (Previously presented) The retroviral vector according to claim 1 wherein the vector is a murine oncoretrovirus vector or a lentivirus vector.

22. (Previously presented) The retroviral vector according to claim 21 wherein the vector is a MMLV, MSV, MMTV, HIV-1 or EIAV retroviral vector.

23-46. (Cancelled)

47. (Currently amended) A method of producing a retroviral vector comprising a functional splice donor site within its 5' long terminal repeat (LTR), the method comprising:

(a) ~~providing~~ introducing, into a packaging cell, a retroviral pro-vector comprising:

(i) a 3' and 5' LTR;

(ii) a functional splice donor site located within the 3' LTR;

(iii) a functional splice acceptor site upstream of the splice donor site;

(iv) a first nucleotide sequence of interest (NOI) upstream of the functional splice acceptor site, wherein the first NOI comprises a packaging signal; and

(v) a second NOI downstream of the functional splice acceptor site and upstream of the 3' LTR,

wherein the retroviral pro-vector is packaged into a viral particle in the packaging cell; and

(b) ~~packaging the retroviral pro-vector in a packaging cell, thereby producing a viral particle; and~~

~~(c)~~ infecting a target cell with the viral particle, wherein the retroviral pro-vector is reverse transcribed;

thereby producing a retroviral vector comprising a functional splice donor site within its 5' LTR.

48. (Cancelled)

49. (Previously presented) The method according to claim 47 wherein the first NOI is expressed in the packaging cell.

50. (Currently amended) The method according to claim 47 wherein the first NOI further comprises [[is]] a selectable marker or a viral element.

51. (Currently amended) The method according to claim 50 wherein the viral element is ~~a retroviral packaging signal,~~ a retroviral envelope sequence~~, or a combination thereof~~.

52. (Cancelled)

53. (Previously presented) The method according to claim 47 wherein the retroviral pro-vector is a murine oncoretrovirus pro-vector or a lentivirus retroviral pro-vector.

54. (Previously presented) The method according to claim 53 wherein the retroviral pro-vector is a MMLV, MSV, MMTV, HIV-1, or EIAV retroviral pro-vector.

55. (Currently amended) The method according to claim 47 wherein the retroviral pro-vector comprises a ~~heterologous~~ non-retroviral transcriptional control sequence upstream of the functional splice donor site.

56. (Cancelled)

57. (Currently amended) A retroviral vector comprising:

(a) a 3' and 5' long terminal repeat (LTR);

(b) a functional splice donor site located within the 5' LTR;

(c) a functional splice acceptor site located downstream of the functional splice donor site; and

(d) an NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;

whereby an intervening sequence between the functional splice donor site and the functional splice acceptor site spliced out of RNA transcribed from the retroviral vector ~~removed as a result of splicing~~.

58. (Cancelled)

59. (Previously presented) A retroviral vector comprising a functional splice donor site within its 5' LTR, wherein the retroviral vector is produced by the method of claim 47.

60. (Currently amended) The method according to claim 55, wherein the ~~heterologous~~ transcriptional control sequence is an internal promoter.

61. (Currently amended) The method according to claim 55, wherein the ~~heterologous~~ transcriptional control sequence is located in the 5' LTR.

62. (Currently amended) The method according to claim 55, wherein the ~~heterologous~~ transcriptional control sequence is located in the 3' LTR.

63. (Previously presented) The retroviral vector according to claim 57, wherein the intervening sequence comprises a viral element.

64. (Previously presented) The retroviral vector according to claim 63, wherein the viral element is a packaging signal.

65. (Previously presented) The retroviral vector according to claim 57, wherein the functional splice donor site is from a virus.

66. (Previously presented) The retroviral vector according to claim 57, wherein the functional splice donor site is from an intron.

67. (Previously presented) The retroviral vector according to claim 66, wherein the intron is the small t-intron of SV40 virus.

68. (Previously presented) The retroviral vector according to claim 57, further comprising a multiple cloning site, wherein the functional splice acceptor site is located upstream of the multiple cloning site.

69. (Previously presented) The retroviral vector according to claim 57, wherein the functional splice acceptor site is from a nucleotide sequence coding for an immunological protein.

70. (Previously presented) The retroviral vector according to claim 69, wherein the immunological protein is an immunoglobulin.

71. (Previously presented) The retroviral vector according to claim 70, wherein the immunoglobulin is from an immunoglobulin heavy chain variable region.

72. (Previously presented) The retroviral vector according to claim 57, wherein the vector is a murine oncoretrovirus vector or a lentivirus vector.

73. (Previously presented) The retroviral vector according to claim 72, wherein the vector is a MMLV, MSV, MMTV, HIV-1 or EIAV retroviral vector.

74. (Currently amended) A method of producing a retroviral vector comprising a functional splice donor site within its 5' LTR, the method comprising:

(a) ~~providing~~ introducing, into a packaging cell, a retroviral pro-vector comprising:

(i) a 3' and 5' LTR;

(ii) a functional splice donor site located within the 3' LTR;

(iii) a functional splice acceptor site;

(iv) a packaging signal upstream of the functional splice acceptor site; and

(v) an NOI downstream of the functional splice acceptor site and upstream of the 3' LTR,

wherein the retroviral pro-vector is packaged into a viral particle in the packaging cell; and

(b) ~~packaging the retroviral pro-vector in a packaging cell, thereby producing a viral particle; and~~

~~(c)~~ infecting a target cell with the viral particle, wherein the retroviral pro-vector is reverse transcribed;

thereby producing a retroviral vector comprising a functional splice donor site within its 5' LTR.

75. (Currently amended) The method according to claim 74, wherein the retroviral pro-vector comprises a ~~heterologous~~ non-retroviral transcriptional control sequence upstream of the functional splice donor site.

76. (Currently amended) The method according to claim 75, wherein the ~~heterologous~~ transcriptional control sequence is an internal promoter.

77. (Currently amended) The method according to claim 75, wherein the ~~heterologous~~ transcriptional control sequence is located in the 5' LTR.

78. (Currently amended) The method according to claim 75, wherein the ~~heterologous~~ transcriptional control sequence is located in the 3' LTR.

79. (Previously presented) A retroviral vector comprising a functional splice donor site within its 5' LTR, wherein the retroviral vector is produced by the method of claim 74.

80. (New) A retroviral pro-vector comprising:

(i) a 3' and 5' LTR;

(ii) a functional splice donor site located within the 3' LTR;

(iii) a functional splice acceptor site upstream of the splice donor site;

(iv) a first nucleotide sequence of interest (NOI) upstream of the functional splice acceptor site, and

(v) a second NOI downstream of the functional splice acceptor site and upstream of the 3' LTR.

81. (New) A retroviral particle comprising the retroviral pro-vector of claim 80.

82. (New) A retroviral pro-vector comprising:

(i) a 3' and 5' LTR;

(ii) a functional splice donor site located within the 3' LTR;

(iii) a functional splice acceptor site;

(iv) an NOI downstream of the functional splice acceptor site and upstream of the 3' LTR.

83. (New) A retroviral particle comprising the retroviral pro-vector of claim 82.